

REMARKS

Reconsideration is requested in view of the foregoing amendments and the following remarks.

The claims are 15 to 44, inclusive.

Claims 23 to 30 are to a non-elected invention.

Claims 15 to 22 have been found allowable.

Claims 1 to 14 have been replaced by claims 31 to 44.

Claims 1 to 14 were rejected under 35 USC 112, first paragraph. The specification was objected to under the same statutory provision.

The present invention pertains to the use of fluorophores or chromophores to tag oligonucleotide fragments and use them to determine the nucleotide sequence in DNA and similar molecules. Since there are four different nucleotides present to be detected, the "classical" case to which the present invention applies involves the use of four tags, each being distinguishable from the others by its spectral characteristics. However, this is not to say that the invention including the claims must be limited to the "classical" case. It is clear that one may use the present invention and detect just the one type (out of the four) nucleotide present in the oligonucleotide being sequenced. The advantages of the present invention obtain in such a process just as they do in the "classical" case. The claims should not be restricted to the "classical" case which is but the most complete and elaborate application of this invention. The

and is equally sufficient for the simpler case which is but a subset of the "classical" case.

The Examiner's several other remarks, as we understand them, go to the point that the claims should indicate that in the tags are spectrally distinguishable, that is, the basis for detection of nucleotides in any given sequence undergoing analysis. The claims have been amended, see claims 31 to 40, 43 and 44.

The Examiner also states that the claims are enabled only for the coupling methods described in United States Patent No. 4,849,513. The coupling methods disclosed in the patent are illustrative of the best known ways of practicing the invention. However, it would defeat the purpose of applying for a patent if the claims were to be restricted to these specific coupling methods. We particularly point out that the present invention is directed to detecting the sequence in which nucleotides are found in oligonucleotide fragments. The coupling methods per se are not claimed in this invention.

The rejection under Section 112 should be withdrawn.

Claims 1 to 6, now claims 31 to 36, were rejected over Kaplan, et al. U.S. Patent No. 4,318,846 and Maxim and Gilbert/Sanger in view of Khanna, et al. U.S. Patent No. 4,151,005.

We have extensively discussed and analyzed this prior art in the Amendment filed April 16, 1990. See pages 6 to 13 thereof which is incorporated by reference. In response, the

thereof which is incorporated by reference. In response, the Examiner stated that "It is not taught in either reference that substitution of an non-radiocompound is favorable over radiolabeled tags but it is well understood within the art that any methods that substitute radiolabels with other tags are preferred for reasons that are health related."

The present invention provides major advances in the art which are in no way health related. A major result of the present invention is that it can readily be automated. The sequencing of the entire E.coli genome (3×10^6 base pairs) has now become feasible. This invention has made it possible to begin to think about determining the sequence of extensive stretches of the human genome which contains 3×10^9 base pairs. The prior art radiolabel method using autoradiograms requires contact with the gel and is much too slow to enable full scale analysis of the human genome. These major advances provided by this invention are indicative of its non-obviousness.

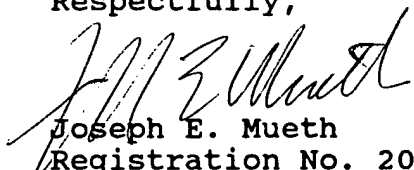
It is true that colored labels and fluorescent labels have been known and used in other processes. These facts serve to demonstrate that the present invention was not obvious to those skilled in the art for, had the use of colored, fluorescent and similar labels been obvious to use in DNA sequencing, it would have been done long ago. The benefits of using these labels in DNA sequencing are undeniable, and so desirable that everyone would have jumped on the colored label-fluorescent label handwagon many years ago, had it been obvious to do so. These

circumstances are powerful evidence that the present invention was not obvious.

The rejection on prior art should be withdrawn.

In the absence of pertinent prior art, the Notice of Allowance is requested.

Respectfully,

A handwritten signature in dark ink, appearing to read "J. E. Mueth", is written over the typed name.

Joseph E. Mueth
Registration No. 20,532

333 South Grand Avenue
Thirty-Seventh Floor
Los Angeles, CA 90071-1599

(213) 688-7407